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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,160	01/15/2007	Eric W. Brunskill	CHM-017	5911

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EXAMINER	
MONTANARI, DAVID A	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,160	BRUNSKILL ET AL.	
	Examiner	Art Unit	
	David Montanari	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 10-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 10-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants arguments and amendments filed on 5/28/2009 have been entered.

2. Claims 18 and 19 are new.

3. Claims 1-6 and 10-19 are examined in the instant application.

Claim Rejections - 35 USC § 101

Claims 1-6 and 10-17 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for reasons of record in the office action mailed on 11/28/2008.

Response to Arguments

Applicants Arguments

Applicants argue in amendment filed on 5/28/2009 that the specification states at the beginning of paragraph 0065 that the claimed Npas3 knock-out mouse is a model of schizophrenia. Applicants continue that the specification also states in paragraph 0117 that potentially therapeutic agents for schizophrenia or related neurological disorders can be administered to Npas3-/- mice to evaluate and interpret their response or performance on specific behavioral tests or biochemical assays. Applicants continue that they have identified a particular transgenic mouse (Npas3-/-) and have identified and demonstrated particular behavioral phenotypes of the mouse, and have explained how those behavioral phenotypes can be used to model the symptoms of a specific mental disorder, namely schizophrenia, and therefore Applicants' description does not contain an assertion of specific and substantial utility for the

invention, and therefore does not fully comply with 35 USC 101. Applicants note that the MPEP Guidelines cited by the Examiner

references transgenic mice, but gives only the example of the transgenic mice as "snake food" as neither a specific (since all transgenic mice could function as snake food) nor substantial (using an expensive transgenic mouse as snake food is not a "real world" context use). Applicants argue that the claimed invention describes a specific and substantial statement of utility, not withstanding any doubt or alleged lack of credibility offered by the Examiner.
Applicants continue that the description supports the statement of specific and substantial utility with the following:

1. the then-recent identification of schizophrenic patients with a deletion of the Npas3 gene (paragraphs [0011] and [0067]);

2. the showing that the neuroimaging of the brains of schizophrenic patients revealed characteristic abnormalities that also found in the brains of the Npas3-/- mice (paragraph [0080]); and

3. the demonstration that the Npas3-/- display the abnormal behavioral phenotypes associated with other mouse models of schizophrenia (beginning at paragraph [0081]), as compared to wild type.

Applicants continue that the law also states that the applicant only needs to show a reasonable correlation between the asserted behavioral phenotype of the knockout mouse and the asserted utility and are not required to show with certainty. Applicant continue that they can establish this reasonable correlation by relying on statistically relevant data documenting the

behavioral phenotypes of the claimed Npas3-/- mouse, arguments or reasoning, documentary evidence (e.g., Applicants' articles in scientific journals), or any combination thereof. Applicant continues that they do not have to prove that a correlation exists between a particular behavioral phenotype and an asserted use of the Npas3-/- mouse for assessing therapeutic compounds for the treatment of schizophrenia as a matter of statistical certainty, nor do they have to provide actual evidence of success in treating humans where such a utility is asserted.

Applicants continue that the description teaches that the claimed transgenic mouse displays phenotypes that are clearly not generally applied to "any knockout mouse" and that the abnormal behavioral phenotypes displayed by the claimed transgenic mouse are not displayed in the wild-type mouse, and thus the asserted behavioral phenotypes are a result of the KO Npas3 gene. Applicants continue that they are not claiming the Npas3 gene per se or its structure, but rather a transgenic mouse with a KO of the Npas3 gene, thus function of the Npas3 gene is irrelevant. Applicants conclude that their assertions regarding the behavioral phenotypes and their correlation with symptoms of schizophrenia are credible.

Response

The issue with respect to lack of utility regarding the claimed transgenic mouse involves two issues: 1) that the claimed transgenic mouse exhibits phenotypes that "models" schizophrenia and 2) the lack of any known function of the Npas3 gene. While the claimed transgenic mouse may exhibit symptoms, behaviors and pathology that overlaps with animal models of and patients that suffer from schizophrenia, this does not provide a specific and substantial utility that the claimed transgenic mouse is a "model" for schizophrenia. While Applicant is not claiming the Npas3 gene, the entirety of the claimed invention rests upon its

function or lack thereof, of which there is no known function provided in the art or the specification. Applicant has observed several behavioral phenotypes and neuropathology in transgenic mice that lack Npas3 which correlate with behavioral phenotypes in other animal models of schizophrenia and in neuropathology of schizophrenic patients having an Npas3 mutation. However none of these correlations provide a specific or substantial utility to the claimed transgenic mouse since they do not model the disease schizophrenia.

Applicants have knocked out a gene of unknown function and observed several phenotypes. These phenotypes appear to be similar to phenotypes that occur in patients of schizophrenia, however these phenotypes are also not specific to patients with schizophrenia and occur in many other transgenic animals as explained in the enablement rejection below. Applicants, based upon their observations, are claiming that the transgenic mouse will model phenotypes of schizophrenia based upon the disruption of an unknown gene. At the time of filing substantial experimentation would be required to 1) determine the function of the Npas3 gene and 2) establish that the claimed phenotypes clearly and reproducibly model those phenotypes that occur in schizophrenic patients. The skilled artisan at the time of filing would not know how to use the claimed transgenic mouse to model and compare phenotypes of schizophrenia given that the claimed phenotypes are not specific to schizophrenia and often occur in KO animal models as set forth in the enablement rejection below. Thus for the reasons above and of record the rejection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 10-17 remain rejected and new claims 18 and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record in the office action mailed on 11/28/2008.

Response to Arguments

Applicants Arguments

Applicants argue in amendment filed on 5/28/2009 that the rejection was asserted against the set of claims originally filed and not the current set of claims pending, which were presented in a preliminary amendment filed on 2/13/2006. Applicants continue that since claim 1 was amended in the preliminary amendment, the rejection is per se as based upon the wrong set of claims. Applicants request reconsideration of the rejection in view of the obvious differences between the present claims and the claim set incorrectly considered by the Examiner.

These arguments are not persuasive.

Response

The instant enablement rejection is over the amended claims listed in the preliminary amendment filed on 2/13/2006. The originally (unamended) claims filed on 2/13/2006 do not recite the word "schizophrenia", however the basis of the entire rejection is over the lack of enablement of a transgenic mouse that exhibits a phenotype that models schizophrenia, thus the pending rejection is over the claims listed in preliminary amendment filed on 2/13/2006. Further

on pg. 7 of the Non-Final rejection mailed on 11/28/2008 the second paragraph recites that the "The breadth of the claims encompasses a transgenic knockout mouse which models schizophrenia". It was clearly stated that the breadth of the "claims" were considered, and not the limitations and teachings provided for in the specification. Lastly claims 1-12 are recited in the originally filed claims, whereas claims 1-6 and 10-17 were listed (and rejected) in the preliminary amendment. Regarding new claims 18 and 19, these claims would also be rejected for the same reasons set forth in the pending enablement rejection.

To reiterate, the previous enablement rejection set forth that the claimed transgenic mouse is not enabled since the phenotypes claimed could commonly occur in any KO transgenic mouse. Phenotypes such as impaired pre-pusle inhibition, impaired locomotor activity and impaired zero maze behavior are not specific to just schizophrenia and often occur as a side effect of the KO process. The enablement rejection set forth that the genetic background of the KO strain significantly influences behavioral phenotypes making it difficult and unpredictable to determine if the phenotypes observed are due to the disrupted gene of interest or to some other effect from the KO process.

Thus for the reasons above and of record the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 is unclear. As the claim is currently written, it appears that there are two transgenic mice being claimed. Lines 2-3 recite "and a homozygous transgenic Npas3 mutant mouse". However a transgenic mouse is already claimed in line 1.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Montanari whose telephone number is (571)272-3108. The examiner can normally be reached on M-Tr 8-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 1-571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Valarie Bertoglio/

Primary Examiner, Art Unit 1632